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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/614,283	07/08/2003	Tsu-An Hsu	8842.0002	2562

22852 7590 09/21/2006

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EXAMINER	
GARVEY, TARA L	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 09/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/614,283	HSU ET AL.	
	Examiner	Art Unit	
	Tara L. Garvey	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,11-14,19,21-26 and 33-41* is/are pending in the application.

4a) Of the above claim(s) *19,25 and 33-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,11-14,21-24 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-5,11-14,19, 21-26 and 33-41 are pending.

Response to Arguments

Applicant's arguments filed July 6, 2006 have been fully considered but they are not persuasive.

In regard to the second non-final office action, the piecemeal prosecution referred to by applicant was not intentional. Rather, the new rejections under 35 U.S.C. § 103(a) were made upon further search and consideration of the claims in order to ensure a thorough and proper examination of the claims for the applicant.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 11-13, 21, 22, 24 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Finkelstein et al (Journal of Biotechnology (1999) volume 75, pages 33-44 referenced in the IDS submitted on September 27, 2004) in view of McMinn, P (FEMS Microbiology Reviews (2002) volume 26, pages 91-107) for reasons of record as set forth in the office action mailed on April 10, 2006.

Applicant's argue that Office has not etablished a prima facie case of obviousness. First, no motivation exists to combine Finkelstein and McMinn and that the motivation to combine must be found in the prior art. The teachings of Finkelstein and McMinn do not provide either alone or in combination motivation to substitue EV71 IRES for the EMCV IRES used by Finkelstein. Further, the applicant's argue that Finkelstein indicates that EMCV IRES was used in the bicistronic baculovirus vector was not as efficient as in mammalina cells, but theorizes that the low levels of expression were the result of low levels of essential factors essential for IRES activity in insect cells or low affinity of the cell factors for EMCV-IRES. Thus, the low levels of expression are a result of the insect cell and not the IRES used. In addition, McMinn does not teach or suggest that the EV71 IRES would provide more efficent expression than the EMCV IRES in any cell type. McMinn only teaches that substitution of EV71 IRES with the IRES in the PV1(M) poliovirus does not reduce the neurovirulence of PV1(M), but does not speculate about the efficiency of the EV71 IRES in supporting internal ribosome entry in any cell type or compare the EV71 IRES to the EMCV IRES.

Thus, McMinn does not teach or suggest that the EV71 IRES would be desirable to use in a bicistronic vector in general or that the EV71 IRES would be more desirable than the EMCV IRES. Finally, the applicant argues that the Office's reliance upon McMinn's teaching that an IRES exists in EV71 is nothing more than an identification of an element of applicant's invention that the Office suggest in hindsight could potentially be substituted into the bicistronic vector of Finkelstein.

Second, McMinn does not provide a reasonable expectation of success that the EV71 IRES would function in a dicistronic expression vector. Applicant's argue that McMinn, either alone or in combination Finkelstein does not provide a reasonable expectation that the EV71 IRES would function as an IRES in a dicistronic expression vector. In addition, McMInn does not directly show that the EV71 IRES functions to permit interanl ribosome entry for protein expression, but only shows that substitution with the IRES in the PV1(M) poliovirus does not reduce neurovirulence of PV1(M). Applicant's further argue that Finkestein teaches that the IRES activity in one vector system does not provide a reasonable expectation that the IRES will be efficient, or even functional, in other expression systems. Thus, even had McMInn shown efficient EV71 IRES activity from a bicistronic vector in poliovirus, those results would not provide reasonable expectation that the EV71 IRES would function in the baculovirus system as part of a bicistronic vector.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention

where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Finkelstein teaches that the inefficiency of EMCV IRES in insect cells may be due to low levels of factors for EMCV IRES activity or to low affinity of the insect cell factors for the EMCV IRES, but Finkelstein does not indicate that this is the case for all viral IRES elements. Therefore, one would be motivated to use a different viral IRES such as the EV71 IRES which has been identified and the EV71 5' UTR region sequenced (see below) to potentially obtain better expression. One of skill in the art routinely substitutes one IRES for another.

In regard to the McMinn reference, McMinn teaches that an IRES has been identified in the 5'UTR EV71. Additionally, the IRES was found to be interchangeable with other viral IRES elements in terms of neurovirulence, which would suggest that if it is functional for neurovirulence that it would be interchangeable for IRES function since it has been identified as an IRES. Further, the 5' UTR of established EV71 strains and isolates from patients have been sequenced as evidenced by AbuBakar, S et al (Virus Research (1999) volume 61 pages 1-9, see abstract, page 2, right column and Table 1, page 3, right column, page 4, left column and pages 4-8, Figure 2), which was cited as reference 77 in McMinn, P.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that

any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Second, in regard to the reasonable expectation of success, McMinn has identified an IRES within 5' UTR of EV71 and the sequence of the 5'UTR of different strains of EV71 have been provided by AbuBakar, S et al. These teachings provide a reasonable expectation that the element identified as an EV71 IRES will function as an IRES. In terms of Finkelstein, Finkelstein has demonstrated that the EMCV IRES was not as efficient in insect cells as mammalian cells, but that enough expression was still obtained for their experiments. Further, the result of the difference was the cell type and not the IRES vector system itself.

Claims 1-5, 11-13, 21, 22, 24 and 26 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Finkelstein et al (Journal of Biotechnology (1999) volume 75, pages 33-44 referenced in the IDS submitted on September 27, 2004) in view of McMinn, P (FEMS Microbiology Reviews (2002) volume 26, pages 91-107) for reasons of record as set forth in the office action mailed on April 10, 2006 and above.

Claims 1-5, 11-13, 21- 24 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Finkelstein et al (Journal of Biotechnology (1999) volume 75, pages

33-44 referenced in the IDS submitted on September 27, 2004) and McMinn, P (FEMS Microbiology Reviews (2002) volume 26, pages 91-107) in further view of Urabe et al (Gene (1997) volume 200, pages 157-162; made of record in the office action mailed September 22, 2005) for reasons of record as set forth in the office action mailed on April 10, 2006.

Applicant's argue that as discussed previoulsy Finkelstein in view of McMinn does not provide the ordinary artisan with the motivation to use the EV71 IRES in a bicistronic vector for baculovirus. The teaching of Urabe that an IRES can be used to express a therapeutic gene does not remedy the deficiencies in in Finkelstein and McMinn.

In response to applicant's arguments, the applicant's arguments regarding the combination of Finkelstein and McMinn have been addressed previously.

Claims 1-5, 11-13, 21- 24 and 26 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Finkelstein et al (Journal of Biotechnology (1999) volume 75, pages 33-44 referenced in the IDS submitted on September 27, 2004) and McMinn, P (FEMS Microbiology Reviews (2002) volume 26, pages 91-107) in further view of Urabe et al (Gene (1997) volume 200, pages 157-162; made of record in the office action mailed September 22, 2005) for reasons of record as set forth in the office action mailed on April 10, 2006 and above.

Claims 1-5, 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Urabe et al (Gene (1997) volume 200, pages 157-162; made of

record in the office action mailed September 22, 2005) in view of McMinn, P (FEMS Microbiology Reviews (2002) volume 26, pages 91-107) for reasons of record as set forth in the office action mailed on April 10, 2006.

Applicant's argue that McMinn's teaching regarding EV71 IRES does not provide reasonable expectation that the EV71 IRES could be used succesfully in a bicistronic vector. Further, Urabe does not mention the EV71 URES and does not remedy the defect in the teachings of McMinn. Further, the applicant's argue that a motivation does not exist to substiitute the EV71 IRES of McMinn for the HCV IRES in the AAV system for expression of a therapeutic gene taught by Urabe. Urabe emphasizes the selection of HCV IRES because of its small size, which permits insertion of larger therapeutic genes into the vector. The 5'UTR containing the EV71 IRES in Figure 1 of the Specification of the instant application is 663 nucleotides in length. Thus, there would have been no motivation tosubstitute a larger EV71 IRES for the smaller HCV IRES.

In response to applicant's arguments, McMinn teaches that an IRES has been identified in the 5'UTR of EV71. Additionally, the IRES was found to be interchangeable with other viral IRES elements in terms of neurovirulence, which would suggest that if it is functional for neurovirulence that it would be interchangeable for IRES function since it has been identified as an IRES. Further, the 5' UTR of established EV71 strains and isolates from patients have been sequenced as evidenced by AbuBakar, S et al (Virus Research (1999) volume 61 pages 1-9, see abstract, page 2, right column and Table 1, page 3, right column, page 4, left column and pages 4-8, Figure 2), which was cited as reference 77 in McMinn, P. Therefore, although the size of the EV71 IRES may be

slightly larger than the HCV IRES, one would be motivated to use a different IRES such as the EV71 IRES which has been identified and the EV71 5' UTR region sequenced to potentially obtain better expression and to also have an alternative IRES to use. One of skill in the art routinely substitutes one IRES for another as demonstrated by Urabe et al in using an alternative IRES from HCV instead of the widely used EMCV IRES (page 157, right column, first full paragraph bridging page 158, left column, line 4).

Claims 1-5, 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Urabe et al (Gene (1997) volume 200, pages 157-162; made of record in the office action mailed September 22, 2005) in view of McMinn, P (FEMS Microbiology Reviews (2002) volume 26, pages 91-107) for reasons of record as set forth in the office action mailed on April 10, 2006 and above.

Claims 1, 3-5, 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over van Zonneveld et al (US 6,447,768; made of record in the office action mailed September 22, 2005) in view of McMinn, P (FEMS Microbiology Reviews (2002) volume 26, pages 91-107) for reasons of record as set forth in the office action mailed on April 10. 2006.

Applicant's argue that van Zonneveld provides no teaching or suggestion that the EMCV IRES used in the bicistronic vector should be substituted. Further, the Office has not provided any rationale for its proposed substitution beyond alleging that McMInn suggest that the EV71 IRES would provide efficient expression and McMinn's teachings

do not reasonably suggest that the EV71 IRES would lead to efficient expression in any bicistronic vector system.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, McMinn teaches that an IRES has been identified in the 5'UTR of EV71. Additionally, the IRES was found to be interchangeable with other viral IRES elements in terms of neurovirulence, which would suggest that if it is functional for neurovirulence that it would be interchangeable for IRES function since it has been identified as an IRES. Further, the 5' UTR of established EV71 strains and isolates from patients have been sequenced as evidenced by AbuBakar, S et al (Virus Research (1999) volume 61 pages 1-9, see abstract, page 2, right column and Table 1, page 3, right column, page 4, left column and pages 4-8, Figure 2), which was cited as reference 77 in McMinn, P. Therefore, one would be motivated to use a different IRES such as the EV71 IRES which has been identified and the EV71 5' UTR region sequenced to potentially obtain better expression and to also have an alternative IRES to use. One of skill in the art routinely substitutes one IRES for another.

Claims 1, 3-5, 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over van Zonneveld et al (US 6,447,768; made of record in the office action mailed September 22, 2005) in view of McMinn, P (FEMS Microbiology Reviews (2002) volume 26, pages 91-107) for reasons of record as set forth in the office action mailed on April 10, 2006 and above.

Claims 1, 3-5, 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Whitley et al et al (US 6,764,675; made of record in the office action mailed September 22, 2005) in view of McMinn, P (FEMS Microbiology Reviews (2002) volume 26, pages 91-107) for reasons of record as set forth in the office action mailed on April 10. 2006.

Applicant's argue that the teachings of Whitley use a commercially avalible IRES and do not indicate any reason to replace the commercial IRES with an IRES frm another source. Further, as previously discussed, McMinn does not reasonably suggest that the EV71 IRES would lead to efficient expression in any bicistronic vector system. Thus, this combination does not provide any motivation to make the substitution proposed by the Office.

In response to applicant's arguments, McMinn teaches that an IRES has been identified in the 5'UTR of EV71. Additionally, the IRES was found to be interchangeable with other viral IRES elements in terms of neurovirulence, which would suggest that if it is functional for neurovirulence that it would be interchangeable for IRES function since it has been identified as an IRES. Further, the 5' UTR of established EV71 strains and

isolates from patients have been sequenced as evidenced by AbuBakar, S et al (Virus Research (1999) volume 61 pages 1-9, see abstract, page 2, right column and Table 1, page 3, right column, page 4, left column and pages 4-8, Figure 2), which was cited as reference 77 in McMinn, P. Therefore, one would be motivated to use a different IRES such as the EV71 IRES which has been identified and the EV71 5' UTR region sequenced to potentially obtain better expression and to also have an alternative IRES to use. One of skill in the art routinely substitutes one IRES for another.

Claims 1, 3-5, 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Whitley et al et al (US 6,764,675; made of record in the office action mailed September 22, 2005) in view of McMinn, P (FEMS Microbiology Reviews (2002) volume 26, pages 91-107) for reasons of record as set forth in the office action mailed on April 10, 2006 and above.

Claims 1-5, 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Agarwal et al (US 6,194,212; made of record in the office action mailed September 22, 2005) in view of McMinn, P (FEMS Microbiology Reviews (2002) volume 26, pages 91-107) for reasons of record as set forth in the office action mailed on April 10. 2006.

Applicant's argue that McMinn does not provide a reasonable expectation that the EV71 IRES can be used in the bicistronic vector and Argarwal does not remedy this defect. Futher, Argarwal does not raise any concerns about the expression obtained frm its IRES vector and therfore, this reference either alone or in combination with

McMinn does not provide any reason to substitute the EV71 IRES for the IRES used by Agarwal. There is neither motivation to replace the IRES used in the vectors of the primary reference with the EV71 IRES nor a reasonable expectation of success that EV71 would function if the substitution were made.

In response to applicant's arguments, McMinn teaches that an IRES has been identified in the 5'UTR of EV71. Additionally, the IRES was found to be interchangeable with other viral IRES elements in terms of neurovirulence, which would suggest that if it is functional for neurovirulence that it would be interchangeable for IRES function since it has been identified as an IRES. Further, the 5' UTR of established EV71 strains and isolates from patients have been sequenced as evidenced by AbuBakar, S et al (Virus Research (1999) volume 61 pages 1-9, see abstract, page 2, right column and Table 1, page 3, right column, page 4, left column and pages 4-8, Figure 2), which was cited as reference 77 in McMinn, P. Therefore, one would be motivated to use a different IRES such as the EV71 IRES which has been identified and the EV71 5' UTR region sequenced to potentially obtain better expression and to also have an alternative IRES to use. One of skill in the art routinely substitutes one IRES for another.

Claims 1-5, 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Agarwal et al (US 6,194,212; made of record in the office action mailed September 22, 2005) in view of McMinn, P (FEMS Microbiology Reviews (2002) volume 26, pages 91-107) for reasons of record as set forth in the office action mailed on April 10. 2006 and above.

Claims 1, 3-5, 11 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seguela et al (US 2003/0219858; made of record in the office action mailed September 22, 2005) in view of McMinn, P (FEMS Microbiology Reviews (2002) volume 26, pages 91-107) for reasons of record as set forth in the office action mailed on April 10. 2006.

Applicant's argue that Seguela does not provide a reason to replace the commercial IRES with an IRES from another source in the same manner argued for the combination of Whitley and McMinn.

In response to applicant's arguments, McMinn teaches that an IRES has been identified in the 5'UTR of EV71. Additionally, the IRES was found to be interchangeable with other viral IRES elements in terms of neurovirulence, which would suggest that if it is functional for neurovirulence that it would be interchangeable for IRES function since it has been identified as an IRES. Further, the 5' UTR of established EV71 strains and isolates from patients have been sequenced as evidenced by AbuBakar, S et al (Virus Research (1999) volume 61 pages 1-9; see abstract, page 2, right column and Table 1, page 3, right column, page 4, left column and pages 4-8, Figure 2), which was cited as reference 77 in McMinn, P. Therefore, one would be motivated to use a different IRES such as the EV71 IRES which has been identified and the EV71 5' UTR region sequenced to potentially obtain better expression and to also have an alternative IRES to use. One of skill in the art routinely substitutes one IRES for another.

Claims 1, 3-5, 11 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seguela et al (US 2003/0219858; made of record in the office action

mailed September 22, 2005) in view of McMinn, P (FEMS Microbiology Reviews (2002) volume 26, pages 91-107) for reasons of record as set forth in the office action mailed on April 10. 2006 and above.

Claims 1-5, 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kirkegaard et al (US 2004/0052765 A1; made of record in the office action mailed September 22, 2005) in view of McMinn, P (FEMS Microbiology Reviews (2002) volume 26, pages 91-107) for reasons of record as set forth in the office action mailed on April 10. 2006.

Applicant's argue that although McMinn replaces the PV1(M) poliovirus IRES with the EV71 IRES, the substitution is not the functional equivalent of preparing a bicistronic vector because McMinn produced a chimeric virus. Further, McMinn did not assess the ability of the EV71 IRES to provide cap-independent expression of a protein, but rather assayed the effect of neurovirulence on the substitution. Thus, McMinn does not provide a reasonable expectation that the EV71 IRES would function in the ocntext of a bicistronic vector. Further, one would not have been motivated to substitute the EV71 IRES for the IRES used by Kirkegaard because Kirkegaard does not suggest that there are any problems with the poliovirus IRES and McMinn does not suggest that the EV71 IRES is more desirable than the poliovirurs IRES.

In response to applicant's arguments, McMinn teaches that an IRES has been identified in the 5'UTR of EV71. Additionally, the IRES was found to be interchangeable with other viral IRES elements in terms of neurovirulence, which would suggest that if it

is functional for neurovirulence that it would be interchangeable for IRES function since it has been identified as an IRES. Further, the 5' UTR of established EV71 strains and isolates from patients have been sequenced as evidenced by AbuBakar, S et al (Virus Research (1999) volume 61 pages 1-9, see abstract, page 2, right column and Table 1, page 3, right column, page 4, left column and pages 4-8, Figure 2), which was cited as reference 77 in McMinn, P. Therefore, one would be motivated to use a different IRES such as the EV71 IRES which has been identified and the EV71 5' UTR region sequenced to potentially obtain better expression and to also have an alternative IRES to use. One of skill in the art routinely substitutes one IRES for another.

Claims 1-5, 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kirkegaard et al (US 2004/0052765 A1; made of record in the office action mailed September 22, 2005) in view of McMinn, P (FEMS Microbiology Reviews (2002) volume 26, pages 91-107) for reasons of record as set forth in the office action mailed on April 10. 2006 and above.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tara L Garvey whose telephone number is (571) 272-2917. The examiner can normally be reached on Monday through Friday 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) (http://pair-direct.uspto.gov) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution

of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Tara L Garvey, Ph.D.
Examiner
Art Unit 1636

TLG

CELINE QIAN, PH.D.
PRIMARY EXAMINER